REMARKS

Reconsideration and allowance are respectfully requested.

Claims 9-11 are pending. The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. Entry of the amendments is consistent with the Examiner's allegation that only the disclosure of this specification supports the claimed invention and puts this application in better condition for appeal.

Claim for Priority Benefit

Although Applicants disagree with the Examiner's denial of priority benefit, they amend their priority claim in the first paragraph of the specification and withdraw their claim to priority benefit of Application No. 10/137,699. Support for the claimed invention is present in Application No. PCT/IT03/00237 (see Example 5).

Acknowledgment is requested that Applicants' claim of priority benefit is proper.

35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 9-10 were rejected as allegedly anticipated by Mistrello et al. (Immunopharm. 10:163-169, 1985). Applicants traverse.

Applicants' claimed invention requires "treating uveitis in a subject" by "administering 3-(2-ethylphenyl)-5-(3-methoxyphenyl)-1H-1,2,4-triazole to said subject." Thus, the compound is administered to a subject and uveitis in the subject is treated by such administration. The Examiner's allegation on page 4 of the Action (i.e., "Mistrello et al. teach the same method step as claimed in the instant application") is plainly incorrect. Uveitis of the "said subject" is treated in claim 1. Nowhere in the Mistrello et al. document is uveitis treated or is the compound administered to a subject having uveitis.

As previously discussed, Mistrello et al. discloses that the compound of the claim has an immunosuppressive effect on antibody responses, delayed type hypersensitivity, and skin graft rejection activity. But there was no effect of the compound on polyarthritis. The compound was taught at page 168 to be "completely ineffective in suppressing adjuvant-induced arthritis" (i.e., polyarthritis). Thus, the effectiveness of the compound against polyarthritis cannot be inherent as alleged on page 4 of the Action because the compound was demonstrated by Mistrello et al. to be completely ineffective under the conditions studied!

Claim 1 of Patent No. 6,797,722 (the '722 patent) is directed to the treatment of autoimmune diseases such as multiple sclerosis, systemic lupus erythematosus, and rheumatoid arthritis with the same compound as the claims in this application. Applicants submit that multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and uveitis all belong to the genus of autoimmune diseases, but each one is a different disease. It is well accepted that a species of a genus does anticipate a different species even if they both belong to the same genus. *Cats and dogs are both mammals, but a cat is different from a dog and vice versa. In analogy to the genus-species relationship, a cat cannot anticipate a dog.*

Anticipation requires "each and every limitation" to be taught in the same document. Here, the diseases studied by Mistrello et al. do not include uveitis. The cited document attempts to treat polyarthritis, but this disease is not uveitis. Although both polyarthritis and uveitis are autoimmune diseases, they are not the same autoimmune disease. A specific autoimmune disease (e.g., polyarthritis) does not teach a different autoimmune disease (e.g., uveitis). Therefore, to the extent that the Examiner relies on the attempted treatment of polyarthritis in the Mistrello et al. document also to teach treatment of uveitis, Applicants do not agree with this reliance and note that there is no evidence of record that polyarthritis and uveitis are the same disease.

The Kawahito et al. document was cited on pages 4-5 of the Action as "evidence" that the uveitis and polyarthritis treatment groups overlap. But this misunderstands the objectives of the study, its results, and their proper interpretation. Disease susceptibility loci were mapped for collagen-induced arthritis (*Cia*), adjuvant-induced arthritis (*Aia2*

and *Aia3*), and experimental autoimmune uveitis (*Eau*). Rats are susceptible or resistant to these autoimmune diseases based on their inheritance of genes mapping to these loci. Inheritance of a disease susceptibility gene increases the *probability* or *chance* that the disease will occur. But there is no strict correlation between possession of a susceptibility gene and occurrence of disease. Fig. 1b shows that there are rats who carry the susceptibility genes and are not affected by adjuvant-induced arthritis (i.e., a maximum arthritis score of 0). Kawahito et al. admit on page 4417 that they have not "definitively demonstrated" that *Aia3*/*Cia3* and *Eau* are allelic. Further even if they were allelic, this would not prove that the diseases are the same. For example, the Examiner appears to acknowledge on page 6 of the Action that adjuvant-induced arthritis (AIA) and collagen-induced arthritis (CIA) are different diseases since they involve different disease mechanisms. At least some of their disease susceptibility genes, however, apparently map to the same loci even though they are different diseases. Thus, mapping of *Aia* and *Eau* disease susceptibility genes to the same genetic interval (i.e., not necessarily allelic) is not sufficient evidence to prove that polyarthritis and uveitis are the same disease.

But inherency may not be established by probabilities or possibilities. *Continental Can v. Monsanto*, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) *quoting In re Oelrich*, 212 USPQ 323, 326 (CCPA 1981) ("The mere fact that a certain thing may result from a given set of circumstances is not sufficient"). The extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *In re Robertson*, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999) *quoting Continental Can id.* at 1749. Therefore, even if a subject is susceptible to developing both polyarthritis and uveitis, this would prove at most that there is merely a possibility that both diseases are present in the subject (or that a subject treated for polyarthritis would also be treated for uveitis). Both diseases would not necessarily occur in the same subject being treated.

Withdrawal of the Section 102 rejection is requested because the cited document fails to disclose all limitations of the claimed invention.

35 U.S.C. 103 – Nonobviousness

To establish a case of prima facie obviousness, all of the claim limitations must be taught or suggested by the prior art. See M.P.E.P. § 2143.03. A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. In re Kahn, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing the legal standard provided in Graham v. John Deere, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See id. ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See id. at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning"). Thus, a rejection under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of [prima facie] obviousness is correct." *Kahn*, 78 USPQ2d at 1335; see *KSR*, 82 USPQ2d at 1396. An inquiry should be made as to "whether the improvement is more than the predictable use of prior art elements according to their established functions." Id. at 1396. But a claim which is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." Id. at 1396. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claim 11 was rejected as allegedly unpatentable over Mistrello et al. (Immunopharm. 10:163-169, 1985) in view of Mozes et al. (Clin. Immunol. Immunopharm. 85:28-34, 1997). Applicants traverse. The Patent Office's guidelines for determining obviousness in genus-species situations are found at M.P.E.P. 2144.08.

Applicants' claimed invention requires "treating uveitis in a [human] subject" by "administering 3-(2-ethylphenyl)-5-(3-methoxyphenyl)-1H-1,2,4-triazole to said subject." The cited documents fail to teach or suggest treating uveitis in any subject (especially not a human subject). Cf. page 11 of the Action ("Mistrello et al. and Mozes et al. do not teach uveitis"). They also do not teach or suggest treating a human. In contradiction to acceptable principles of logic and causality, the Examiner alleges on pages 7-8 that the ineffectiveness of the compound in treating polyarthritis at doses of 2 mg/kg/day would allow a skilled artisan to "reasonably envision that the administration of an identical dose of DLT111-IT to subjects suffering from uveitis and polyarthritis would necessarily effectuate an immunosuppressive effect in treating both uveitis and polyarthritis." It makes no sense whatsoever that the failure to effectively treat polyarthritis according to the teachings of the Mistrello et al. document would bolster an argument of a reasonable expectation of success to treat uveitis using the immunosuppressive activity of the compound! It certainly would not provide "a reasonable expectation of success that DL111-IT would exhibit immunosuppressive activity in humans suffering from uveitis." Cf. page 11 of the Action. No evidence or reasoning is provided in the Action for extrapolating from the combination of Mistrello et al. and Mozes et al. when neither document teaches or suggests (i) treating uveitis and (ii) treating a human.

In the Mistrello et al. document, the compound was not effective in treating polyarthritis. One of ordinary skill in the art would have understood from this negative result that a reasonable expectation of success was lacking to use the compound as an immunosuppressive agent in treating any autoimmune disease including uveitis. Therefore, there is no reasonable expectation of success provided in Mistrello et al. or in the other evidence of record. But a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rhinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976). Moreover, the requirements of M.P.E.P. 2144.08 are not satisfied for establishing a case of prima facie obviousness in accordance with the guidelines for the examination of claims directed to a species when the reference discloses the genus. Here, Mistrello et al. and Mozes et al. fail to disclose successful treatment of any autoimmune disease in a human or any other subject.

Withdrawal of the Section 103 rejection is requested because the claimed invention would not have been obvious to the ordinarily skilled artisan at the time Applicants made their invention.

35 U.S.C. 112 – Written Description

The specification must convey with reasonable clarity to persons skilled in the art that applicant was in possession of the claimed invention as of the filing date sought. See *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). But the Patent Office has the initial burden of presenting evidence or a reason why persons of ordinary skill in the art would not have recognized such a description of the claimed invention in the original disclosure. See *In re Gosteli*, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

Claims 9-11 were rejected under Section 112, first paragraph, because they allegedly contain "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Applicants traverse because deleting "an effective amount" from the claims does not introduce new matter into the disclosure.

In the Office Action mailed November 29, 2006, the Examiner alleged that "effective amount" is indefinite. In response, Applicants canceled the limitation as not required to define a patentable invention. The present claim is directed to treatment of uveitis in a subject by administering 3-(2-ethylphenyl)-5-(3-methoxyphenyl)-1H-1,2,4-triazole. If the compound was administered under conditions (e.g., the amount or dose) that were not effective then such conditions would not constitute treatment of uveitis. Therefore, only treatment with an effective amount of the compound would necessarily be within the scope of the claims. A specification need not teach, and preferably omits, what is well known in the art. See *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81, 94 (Fed. Cir. 1986). Conditions under which uveitis is treated in accordance with Applicants' invention may be routinely determined and does not require recitation in the claims of specific amounts of the compound.

Original claim 5 requires the treatment of uveitis using the compound. The limitation "effective amount" is not recited in claim 5. See also page 6, lines 2-4, of the specification where treatment of an autoimmune disease is taught without recitation of an effective amount of the compound. A working example of treatment of uveitis in an accepted animal model of the disease is provided on pages 14-15 of the specification. Clearly, support for the presently claimed invention exists in the original disclosure without requiring an effective amount of the compound. Therefore, support for Applicants' invention as presently claimed (i.e., no recitation of an effective amount) exists in the originally-filed disclosure.

Withdrawal of the written description rejection is requested because the specification conveys to a person skilled in the art that Applicants were in possession of the claimed invention as of the filing date.

Conclusion

Having fully responded to all of the pending objections and rejections contained in this Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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